LARGE MAMMALS - THE OVINE MCAO MODEL:
A TOOL FOR TRANSLATIONAL BRAIN ISCHEMIA RESEARCH

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Until now, all alternative substances to overcome the limitations of thrombolysis with rtPA (i.e. limited time window, contraindications) failed in clinical studies after successful preclinical testing in standard rodent models. Therefore, international academic and industrial expert consortia (STAIR, STEPS) suggest stringent preclinical research strategies including validation of novel treatment strategies in gyrencephalic animal models of stroke. However, most existing gyrencephalic animal models are cost expensive, limited due to ethical questions or species specific anatomical restriction. Importantly, most large animal models do not allow long term investigations.

To overcome these limitations, an ovine model of cerebral ischemia by permanent middle cerebral artery occlusion (MCAO) was established. After detailed characterization of the model itself, it was utilized in acute stroke treatment studies, for example using nitrogen monoxide, but also in long term experiments such as assessment of autologous bone marrow cell therapy. Additionally, frameless stereotaxic methods enable local administration of cells and/or substances for different purposes. Moreover, the animal model is routinely used for state-of-the-art imaging studies (MRI and PET) including automatic image processing and analysis using ovine stereotaxic atlas.

Major strengths of the ovine MCAO model comprise reproducible lesion size, capability for long term studies and clinical imaging procedure, as well as relatively low costs. The transcranial approach avoids enucleation, enabling testing of neurological functions without modeling effects, but at the cost of artificial intracranial pressure profiles. The model has also been adopted for transient MCAO.

transstrain MCAO procedures, although only applicable in acute stroke studies so far.